Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Initially, applicants would like to extend their gratitude for the courtesy extended to their undersigned representative during the telephone conference between Examiner Hutson and the undersigned representative on November 6, 2003. The substance of the interview is set forth below.

Because this application has been finally rejected, applicants would like to point out that despite the amendments to the claims and the new claims presented, the total number of pending claims remains at 15 claims.

The objection to the specification has been overcome by the above amendment and should therefore be withdrawn.

Applicants submit that the objection to claims 8 and 9 is overcome by the above amendments. Applicants have amended claim 1 and presented evidence as to why the presently claimed invention is allowable. Therefore, the objection to these claims should be withdrawn.

The rejection of claims 52, 55, and 73 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments and the following remarks.

With respect to the rejection of claim 73 for recitation of the limitation '5X sodium citrate buffer,' the apparent confusion relates to applicants prior usage, i.e., vis-a-vis claims 1 and 73, of both molarity and "5X" for the sodium citrate buffer. This objection is overcome by applicants use of only the 5X designation in claims 1 and 73 as amended. At page 35, line 20, the specification recites the use of a 5X SSC buffer. Moreover, applicants submit that one of skill in the art would understand that this limitation refers to a sodium citrate buffer having a sodium content of 0.825M. As support for applicants' position, attached as Exhibit A is a copy of a product data sheet for 20X SSC buffer available from Ambion, Inc., which indicates that 1X SSC contains 0.15M sodium chloride and 0.15 mM sodium citrate, for a total sodium content of 0.165M. 5X SSC contains five times the content of the 1X SSC buffer, or 0.825M sodium. Thus, one of skill in the art would understand the meaning of the term '5X SSC' presently recited in claims 1 and 73.

The rejection of claims 1, 7, 49-52, 55, and 71-76 under 35 U.S.C. § 112 (first paragraph) as lacking enablement is rendered moot with respect to claims 71, 72, 75, and 76 and is respectfully traversed with respect to claims 1, 7, 49-52, 55, 73, and 74.

The U.S. Patent and Trademark Office has taken the position that despite the teachings of the present application (i.e., the performing of hybridization procedures using the recited conditions, the purification and isolation of recombinant proteins, and assessing whether the isolated protein is able to form a clamp loader), the present application fails to enable the claimed invention. The basis asserted for this position is that guidance is needed to assess which nucleic acids, capable of hybridizing under the claimed conditions, also encode a protein having activity as a delta subunit (office action at page 7). Applicants disagree.

It is well established law that a specification may be enabling though some experimentation is required; the critical factor is whether the level of experimentation rises to a level where it becomes "undue experimentation." *In re Wands*, 858 F.2d 731, 736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Thus, the specification should provide "...a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.* at 737 (citing *In re Jackson*, 217 USPQ 804, 807 (Bd. App. 1982)).

Contrary to the PTO's assertion that the present application must present additional guidance as to whether a particular hybridizing nucleic acid does or does not encode a delta subunit, applicant submits that one of ordinary skill in the art would expect hybridizing nucleic acid molecules to encode such a polypeptide given the hybridization conditions recited in claims 1 and 73 and the requirement that a claimed nucleic acid molecule encode a delta subunit that forms a clamp loader (with delta prime and tau subunits). Because the encoded polypeptide is one that functions as a delta subunit, one of skill in the art would only look to those hybridizing nucleic acid molecules that appear to be full or nearly full length (i.e., hybridizing over substantially the entire length of the complement to SEQ ID NO: 157). As a result of such hybridization, one of ordinary skill would also expect the hybridizing nucleic acid to encode a polypeptide that functions as a delta subunit.

To confirm whether the hybridizing nucleic acid molecule does, in fact, encode a polypeptide that functions as a delta subunit, one of skill in the art need only recombinantly express the polypeptide, isolate the polypeptide, and then test the polypeptide in a clamp loader assay of the type disclosed in the present application. The recombinant expression and isolation of an encoded polypeptide is routine for someone of skill in the art, and performance of the clamp loader assay is easily carried out in accordance with the

description provided at Example 24. Thus, the present invention fully enables one of ordinary skill in the art to obtain a nucleic acid within the scope of the presently claimed invention and, given the expectation that such nucleic acid will encode a polypeptide that functions as a delta subunit, one of ordinary skill in the art can obtain the encoded polypeptide and assay the polypeptide for clamp loader formation. This effort, though requiring several steps, hardly rises to the level of undue experimentation.

With respect to claim 74 as amended (and new claims 77-80 dependent thereon), applicants submit that the above reasons also support the enablement of the claim language presented. Much like the stringency of the hybridization conditions recited in claims 1 and 73, the limitation reciting about 90 percent identity at the nucleic acid level would reliably allow one of ordinary skill in the art to expect the protein encoded by such nucleic acid to be a functional delta subunit.

As further evidence that the presently application does, in fact, enable the presently claimed invention, applicants refer to PCT application US01/09950 (publication WO 01/73052) to McHenry et al. ("McHenry") (partial copy attached as Exhibit B). In particular, at Figures 13 and 14, the nucleotide and amino acid sequences, respectively, of a *Thermus thermophilus* delta subunit are disclosed. The undersigned has performed a Clustal W sequence alignment, using the server at the European Molecular Biology Laboratory Internet site (http://www.embl-heidelberg.de) set on default settings, between the nucleotide sequence of SEQ ID NO: 157 and the nucleotide sequence of McHenry Figure 13. A copy of the Clustal W alignment is attached hereto as Exhibit C. This alignment demonstrates that the two sequences are about 97 percent identical over the length of SEQ ID NO: 157.

Because *Thermus thermophilus* nucleic acid molecules encoding polypeptides that function as delta subunits would be expected to possess a high identity at the nucleic acid level (as the nucleic acid of McHenry demonstrates), such nucleic acids would be expected to hybridize under the various conditions recited in claims 1 and 73. As such, one of skill in the art would fully understand these nucleic acid molecules to fall within the scope of the presently claimed invention.

For all the reasons above, the above-presented evidence supports the conclusion that the present application fully enables the invention of claim 1 and 74. The rejection of claims 1, 7, 49-52, 55, and 71-76 for lack of enablement should therefore be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: November 7, 2003

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